



Seizure disorders: Part 1. Classification and diagnosis

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EPIDEMIOLOGY

- Seizures are the most common acute neurologic problem in the United States
- Epilepsy (recurrent seizures) is the third most common serious neurologic disorder, following stroke and Alzheimer's disease.
- The age-adjusted incidence of newly diagnosed epilepsy is 44 per 100,000 person-years.
- The incidence of epilepsy increases with advanced age; people over 75 are twice as likely to develop new-onset epilepsy as all adult age groups under 65.¹
- By age 74, 3% of all people will have had epilepsy at some point in their lives. For those living to 85, the cumulative incidence rises to 4.4%.¹
- The prevalence of active epilepsy is 0.68%. The prevalence of all unprovoked seizures (including epilepsy) is 0.82%.²

CLASSIFICATION OF SEIZURES^{3,4}

Partial (focal) seizures

- These seizures account for almost 60% of new cases of epilepsy.²
- *Simple partial seizures* occur in about 15% of patients with seizures. Depending on the area of cerebral cortex involved, symptoms may be motor, cognitive, sensory, autonomic, or affective. Consciousness is not impaired.
- *Complex partial seizures*, also known as temporal lobe or psychomotor seizures, occur in approximately 35% of patients with seizures. Consciousness is partially or completely impaired, but there is no initial generalized tonic-clonic activity. Clinical presentation is variable, but patients usually experience an aura, automatism, postictal confusion, or tiredness. They have no memory of the events during the seizure.
- *Partial seizures evolving to generalized seizures* begin locally but then generalize.

Terminology

- **Seizure:** an uncontrolled, paroxysmal neuronal discharge in any part of the brain; it may cause physical or mental symptoms and may be convulsive or nonconvulsive
- **Convulsion:** involuntary contraction of body muscles
- **Epilepsy:** two or more unprovoked, recurrent seizures. Seventy-five percent of epilepsy is primary (idiopathic); 25% is secondary to another CNS disorder.¹
- **Simple seizure:** no alteration of consciousness
- **Complex seizure:** alteration of consciousness
- **Status epilepticus:** epileptic seizures that last more than 30 minutes or occur so frequently that consciousness is not restored between seizures

¹ Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935-1984. *Epilepsia* 1993;34:453-67.

² Hauser WA, Annegers JF, Kurland LT. Prevalence of epilepsy in Rochester, Minnesota: 1940-1980. *Epilepsia* 1991;32:429-444. Long-term population-based studies characterizing 880 patients.

³ The Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised clinical and electroencephalographic classification of epileptic seizures. *Epilepsia* 1981;22:489-501.

This system classifies seizures by clinical symptoms and is easy to use. Another widely used but more complicated system classifies epileptic "syndromes" and includes other data such as family history, exposure history, physical examination, electroencephalography (EEG), imaging, and biochemical studies.

⁴ The Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia* 1989;30:389-99.

Generalized seizures

- These seizures account for 40% of patients with epilepsy.²
- Initial manifestations indicate involvement of both hemispheres, most commonly impairment of consciousness with bilateral motor involvement.
- Patients usually forget the events of the seizure.

Types and characteristics

- Six types of generalized seizures and their presenting signs are described in table 1
- Absence (petit-mal) seizures occur in 5% of patients with seizures, primarily in children
- Tonic-clonic (grand-mal) seizures occur in 25% of all patients with seizures and are the most common type of generalized seizure in adults.

Distinguishing secondarily generalized partial seizures from primary generalized seizures⁵

- Many patients with partial seizures that generalize incorrectly report their seizures as “grand mal.”
- Distinguishing factors favoring secondarily generalized partial seizures are as follows:
 - Preceding the seizure: period of unresponsiveness and staring, aura, automatisms, focal motor phenomena
 - Past occurrence of any of the above factors without impairment of consciousness
 - Focal findings on neurologic examination, magnetic resonance imaging (MRI)
 - Focal activity on the electroencephalogram (EEG)
 - Adult onset of seizures

DIAGNOSIS

General approach

For a first seizure, it is important to distinguish between an isolated event that is caused by an unusual stress, such as alcohol withdrawal, high fever, or hypoglyce-

Historical references

Epilepsy in Ancient Babylon

“If at the time of his fit he loses consciousness and foam comes from his mouth, it is *miqtu* (the falling disease: epilepsy).”

“If a death-wail sounds forth from him and (at each wail) he himself responds to it, rising and falling onto his knees, a demon from the desert has possessed him.”

Text from the 25th and 26th tablets of the *Sakikku*, (“All Diseases”), circa 700 BC. *Kinnier Wilson JV, Reynolds EH. Translation and analysis of a cuneiform text forming part of a Babylonian treatise on epilepsy. Med Hist 1990;34:185-198*

Epilepsy in the Gospels

Here too epilepsy is explained as possession by demons. “When the spirit seizes him, the patient suddenly cries out, falls to the ground, foaming, and grinding the teeth. *Luke 9:39*.

⁵ Mosewich RK, So EL. A clinical approach to the classification of seizures and epileptic syndromes. *Mayo Clin Proc* 1996;71:405-414.

Table 1 Types and characteristic signs of generalized seizures

Type of seizure	Characteristic signs
Absence (petit-mal)	Staring or eye flickering Some body movements may occur No convulsions or postictal symptoms
Myoclonic	Symmetric jerking of the extremities
Clonic	Rapid, repetitive motor activity
Tonic	Rigidity
Tonic-clonic (grand-mal)	Tonic stiffening (extension) followed by clonic flexion motions May produce labored respirations, cyanosis, incontinence, involuntary tongue biting (sensitive but not specific sign), and postictal confusion, fatigue, or stupor
Atonic	Sudden loss of postural tone

mia, and an unprovoked event that may be the initial manifestation of a recurrent seizure disorder (epilepsy).

- Classify the seizure according to abovementioned categories based on available historical information. Reports from eyewitnesses are helpful. Diagnostic classification is necessary for appropriate therapy.
- Evaluate and test for common precipitants (see subsequent list) or unusual causes of seizures on the basis of history and findings from physical examination, blood tests, and imaging, as indicated. Approximately 75% of seizures are idiopathic.
- Consider electrolyte disturbances, hypoglycemia, and withdrawal syndromes (eg, alcohol, benzodiazepines).
- Consider systemic diseases that may cause seizures: renal failure, hepatic failure, systemic lupus erythematosus, AIDS, and porphyria.

Basic evaluation

- Blood tests should include values for glucose, sodium, calcium, and magnesium.
- EEG may determine the presence of an epileptic focus.
- The standard 21-lead, 30-minute recording may be falsely negative; it has a sensitivity of only 50% to 60%.⁶ A 24-hour EEG may be necessary to establish a diagnosis.
- Computed tomography (CT) of the head with contrast enhancement is particularly useful in the setting of a focal seizure, neurologic deficit, possible trauma, or absence of a history of alcohol misuse. CT is also useful in patients with a history of alcohol abuse, but the likelihood of finding an abnormality is less than in other patients with seizures.⁷
- MRI of the head is indicated after a tonic-clonic seizure. MRI will show an abnormality in 10% to 20% of patients with a generalized tonic-clonic seizure and a normal CT scan.⁸
- Lumbar puncture is indicated only if infection or hemorrhage is suspected.

Common etiologies by age²

- 15 to 34 years: 85% idiopathic, 5% post-traumatic, 3% congenital, 3% tumor
- 35 to 64 years: 60% idiopathic, 15% cerebrovascular, 7% post-traumatic, 7% tumor
- 65 years and older: 50% idiopathic, 30% cerebrovascular, 10% degenerative, 4% post-traumatic

Common precipitants

- Emotional stress
- Hyperventilation
- Menstrual cycle
- Sleep deprivation
- Alcohol withdrawal or excess
- Photoc stimulation (strobe lights, television)
- Febrile seizures are very rare in adults

Causes of nonepileptic seizures

- Alcohol withdrawal
- Benzodiazepine withdrawal
- Massive sleep deprivation
- Excessive use of stimulants, cocaine, etc
- Psychogenic (conversion disorder, somatization, factitious disorder, malingering)
- Acute head trauma (within 1 week)
- Central nervous system infection or neoplasm
- Uremia
- Eclampsia
- High fever
- Hypoxemia
- Hyperglycemia or hypoglycemia
- Electrolyte disorders

Neurocysticercosis and malaria are common causes of seizures worldwide and should be considered in patients from high-risk areas.

Classification of epilepsy syndrome based on clinical, EEG, and neuroimaging data

Type of seizure	Clinical alone, %	Clinical + EEG, %	Clinical + EEG + MRI, %
Generalized	8	23	23
Partial	39	54	58
Unclassified	53	23	19

Early EEG, sleep-deprived EEG, and MRI after presentation at first seizure help to categorize seizures that cannot be classified on the basis of clinical information alone. King MA, Newton MR, Graeme D. *Epileptology of the first-seizure presentation: a clinical, electroencephalographic, and magnetic resonance imaging study of 300 patients*. *Lancet* 1998;352:1007-1011.

⁶ Salinsky M, Kanter R, Dashieff RM. *Effectiveness of multiple EEGs in supporting the diagnosis of epilepsy: an operational curve*. *Epilepsia* 1987;28:331-334.

⁷ Schoenenberger RA, Heim SM. *Indication for computed tomography of the brain in patients with first uncomplicated generalized seizure*. *BMJ* 1994;309:986-989. CT revealed a focal lesion in 34% of patients who presented with a first seizure. This affected management in 17% of patients.

⁸ Latack JT, Abou-Khalil BW, Siegel GJ, Sackellares JC, Gabrielsen TO, Aisen AM. *Patients with partial seizures: evaluation by MR, CT and PET imaging*. *Radiology* 1986;159:159-163.

Alcohol withdrawal seizures

- After several years of alcohol dependence, generalized convulsive seizures, single or several in a short series, may begin 7 to 48 hours after cessation of drinking (peak incidence at 13 to 24 hours).
- Abnormalities on EEG may be attributed to the direct effects of alcohol, metabolic disturbances, or previous head trauma.
- CT scanning is indicated, because findings alter management in approximately 4% of cases. Clinically significant lesions include chronic subdural hematomas, subdural hygromas, neurocysticercosis, arteriovenous malformations, and arterial aneurysms.⁹
- If no underlying structural lesion is detected and the patient does not have an epileptic disorder, no antiepileptic drug therapy is indicated. These agents may actually worsen alcohol withdrawal seizures.
- The treatment of choice is aggressive management of alcohol withdrawal for primary prevention of seizures. Intravenous administration of benzodiazepines reduces the risk of recurrent seizures (table 2). The absolute risk reduction for recurrence within 6 hours is 21%.¹⁰

Table 2 Alcohol withdrawal seizure recurrence rate: lorazepam versus placebo*

Treatment	Recurrence in <6 hours, %	Hospital readmission for recurrence, %
Lorazepam	3.0	1.5
Placebo	24	14

*From D'Onofrio et al¹⁰

ESTIMATING RISK OF RECURRENT SEIZURE¹¹

In untreated patients, recurrence after a first seizure occurs in 64% at 6 months, 70% at 1 year, and 81% at 3 years (table 3).

Table 3 Recurrence rate in specific subgroups after first seizure*

Subgroup	6 months, %	1 year, %	3 years, %
Seizure after an acute insult	33	40	46
Seizure after a remote insult	70	75	85
Idiopathic	62	69	81
Vascular process	66	73	82
Tumor	83	83	100
Alcohol	41	48	55
Tonic-clonic	53	60	72
Partial	82	89	94

*From Hart et al¹¹

CT results in patients with alcohol withdrawal seizures (AWS)

Result	Percentage (%) of all patients with AWS
Normal	43
Generalized enlarged cerebrospinal fluid spaces	38
Clinically significant intracranial lesion	6
Anterior cerebellar atrophy	5
Focal brain lesion due to old injury	5
Other clinically insignificant lesion	3

⁹ Earnest MP, Feldman H, Marx JA, et al. Intracranial lesion shown by CT scans in 259 cases of first alcohol related seizures. *Neurology* 1988;38:1561-1565.

¹⁰ D'Onofrio G, Rathlev NK, Ulrich AS, et al. Lorazepam for the prevention of recurrent seizures related to alcohol. *N Engl J Med* 1999;340:915-919. Double-blind trial of 186 patients randomly assigned to receive lorazepam (2 mg IV versus injection of 4 mL of normal saline solution). Patients with moderate or severe alcohol withdrawal were excluded from the trial.

¹¹ Hart YM, Sander JWAS, Johnson AL, Shorvon SD. National General Practice Study of Epilepsy: recurrence after a first seizure. *Lancet* 1990;336:1271-1274. This community-based, observational study of 564 patients included patients who had their first seizure before the study began as well as patients who entered the study at the time of their first seizure. Subgroup analysis of patients who were assessed only prospectively revealed a recurrence rate of 43% at 2 years.

PSYCHOSOCIAL CONSIDERATIONS IN EPILEPTOLOGY¹²

- *Health-related quality of life* scores are significantly lower in patients with epilepsy than in the general public. Seizure frequency is a good predictor of quality of life; patients with no recurrences score close to the general public, but performance declines as seizure frequency rises.
- *Cognitive difficulties* limit effective social and occupational functioning.
- *Cognitive performance* may also be reduced by subclinical seizures. For patients without childhood onset seizures, intelligence is usually otherwise normal.
- *Driving*: Many states require that patients be seizure free for 1 year before they may obtain a driver's license.
- *Alcohol consumption*: Moderate use may be tolerated. Heavy use can exacerbate seizures, especially during withdrawal.
- *Return to work* should be recommended on an individual basis, according to the patient's abilities and needs.
- *Death* from epilepsy is rare. When it occurs, it is attributed to status epilepticus or seizures that occur while driving, swimming, bathing, at great heights, or near dangerous objects.

¹² Leidy NK, Elixhauser A, Vickrey B, et al. Seizure frequency and health-related quality of life. *Neurology* 1999;53:162-166.

Refer patients to the Epilepsy Foundation (1-800-EFA-1000), an excellent resource for group support, information, and counseling.

Patients with epilepsy are protected by the Americans with Disabilities Act.

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